

REMARKS/ARGUMENTS

Claims 1-7 are currently pending in this application. Claims 8-17, 20 and 26-28 are withdrawn and claims 18, 19 and 21-25 have been canceled. Claim 1 is an independent claim and the remaining claims depend from claim 1.

Claim 1 is amended herein to recite that the cells are contained within a polymerized biopolymer matrix. Support for this amendment can be found throughout the specification as originally filed, such as on page 5, lines 2-25. Claim 1 is also amended to recite that the layers are positioned vertically on top of each other and that each layer contacts at least one other layer. Support for this amendment can be found on page 23, lines 1-9, and Figure 9 of the specification. Claim 1 is also amended to replace the term "width" with the term "vertical thickness". Support for this amendment can be found on page 2, lines 11-21, page 21, lines 11-31, page 28, lines 17-33, and Figure 6. Claim 1 is also amended to recite that the cells are distributed throughout the matrix. Support for this amendment can be found on page 18, line 29, through page 20, line 2, of the specification which describes preparing the cell matrix as a solution phase which is mixed several times before polymerization. As a result of the mixing, the cells in the solution phase would be distributed throughout every region of the matrix.

Claim 5 is hereby amended to recite that the first layer is resistant to a shear force of 80 dyne/cm². Support for this amendment can be found on page 25, lines 1-22 of the specification.

New claim 29, which depends from claim 1, is added. Claim 29 recites a microculture having three layers, where one layer comprises endothelial cells, one layer comprises smooth muscle cells, and one layer comprises fibroblasts. Support for this claim can be found of page 11, lines 11-15, of the specification.

It is believed no new matter is added by these amendments.

Claim Objections

The Examiner objected to the claims for containing the trade name MATRIGEL and requested that generic terms be used instead to describe the composition. Accordingly, claim 1 is hereby amended to delete the term "MATRIGEL" and insert the term "laminin". MATRIGEL is well known in the art as a solubilized basement membrane preparation containing extracellular matrix proteins such as collagen and laminin. Thus, it is believed the addition of "laminin" to the claim is supported by the original use of the term MATRIGEL. Additional support for this amendment can be found on pages 27, lines 1-8, of the specification as filed which describes known extracellular matrices including basement membranes and laminin.

Claim rejections under 35 USC 101

The Examiner rejected claims 1-7 under 35 USC 101 because the claim limitations allegedly did not require any manipulation and/or isolation and could reasonably be interpreted as being drawn to products of nature. Claim 1 is amended herein to state that the layers of the microculture comprise polymerized biopolymer matrices, and that the layers are positioned vertically on top of each other so that each layer contacts at least one other layer. It is believed that claim 1 as amended is drawn to a product which must be artificially manipulated in order to be formed and is not found in nature. The remaining claims depend from claim 1 and therefore also incorporate these claim limitations. Accordingly, Applicant requests that the rejections under 35 USC 101 be withdrawn.

Claim rejections under 35 USC 112

The Examiner rejected claims 1-7 under 35 USC 112, second paragraph, for failing to specify the structural relationship between the layers. Claim 1 is amended to specify that the layers are positioned vertically on top of each other and that each layer contacts at least one other layer. As amended, claim 1 provides structural relationships between the layers allowing one to recognize the metes and bounds of the claims. In light of this amendment, Applicant requests that this rejection be withdrawn.

The Examiner also rejected claims 1-7 under 35 USC 112, second paragraph, as being indefinite. The Examiner alleged that the term "cell type" is indefinite; stating that it is unclear what defines and distinguishes a cell type in the present invention. Applicant respectfully disagrees. While adding the term "type" to objects can make them indefinite in other circumstances, the term "cell type" within the biological field has a recognized meaning. Specifically, cell type is known in the art to refer to a cell's morphological or functional classification. The human body has approximately 200 known cell types, for example, fibroblasts, osteoblasts, endothelial cells, smooth muscle cells, and erythrocytes. One skilled in the art would attribute the commonly known meaning within the field to the term "cell type" and view this aspect of the claims as definite. Accordingly, Applicant requests that this rejection be withdrawn

The Examiner also asserted that use of the term "width" in claim 1 is indefinite, in part because the claim does not describe the three dimensional context in which the width is measured. The term "width" is meant to refer to the vertical dimension of the layer, commonly referred to as the thickness. As amended, claim 1 recites the layers are vertically stacked on top of each other and replaces the term "width" with the term "vertical thickness". Support for this amendment can be found on page 2, lines 11-21, page 21, lines 11-31, page 28, lines 17-33, and Figure 6. It is believed this amendment clarifies the three dimensional structure of the layers in the claim, and Applicant requests that this rejection be withdrawn.

The Examiner also asserted that it is unclear what the term "distinct cell type" in claim 2 refers to. Claim 2 is hereby amended to recite that each layer comprises a cell type that is distinct from the cell types in other layers. It is believed this amendment removes any ambiguity from the claim, and Applicant requests that this rejection be withdrawn.

The Examiner also asserted that the term "resistance" in claim 5 is indefinite because the associated shear force is dependent on several undetermined properties.

Claim 5 is hereby amended to recite that the first layer is resistant to a shear force of 80 dyne/cm². It is believed the limitations of amended claim 5 satisfy 35 USC 112, and Applicant requests that this rejection be withdrawn.

Claim rejections under 35 USC 103

Claims 1-7 were rejected under 35 USC 103(a) as being obvious over U.S. 5,776,748 (Singhvi) or U.S. 6,197,575 (Griffith). Applicant respectfully traverses.

To establish a prima facie case of obviousness, there must be some suggestion or motivation to combine or adapt the references; a reasonable expectation of success; and the final combination must teach or suggest all of the claim limitations. See MPEP 2142. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The presently amended claims recite a series of biopolymer layers (each layer less than 1 mm in thickness) placed on top of each other, where each layer comprises cells contained within a polymerized biopolymer matrix. Furthermore, the claims are amended to recite that the cells are distributed throughout the matrix. Applicant submits that the cited references do not teach or suggest all of the limitations of the amended claims.

Singhvi teaches a plurality of monolayer islands containing mammalian, non-contractile cells. The claims as presently amended require a plurality of layers vertically stacked on top of each other so that each layer contacts at least one other layer. Singhvi does not teach or suggest multiple layers stacked on top of each other. Additionally, the monolayer islands disclosed in Singhvi are arranged in a grid formation so that there is no contact between islands. Accordingly, Singhvi does not teach or suggest all of the claim limitations, and this rejection should be withdrawn.

Griffin teaches a perfusion chamber comprising a scaffold layer, such as silicon, having a number of channels. These channels are seeded with cells, such as endothelial and hepatocyte cells, which are then free to attach to the channel surface. It is hoped the cells within the channels provide an accurate model of *in vivo* tissues and organs. Griffith states that the microtissues can be stacked on top of each other; however, Griffith defines these tissues as "an aggregation of cells more or less similar morphologically and functionally." There is no teaching that the stacked tissue layers of Griffith contain polymerized biopolymers or that the cells are contained in a polymerized biopolymer matrix. The extracellular matrix materials disclosed by Griffith are used as a coating to attach the cells to the channel surface but do not appear to be polymerized and do not form a biopolymer matrix that contains the cells. Additionally, Griffith does not disclose that the cells are distributed throughout the entire matrix. For example, Griffith discloses that cells are only present within the channels. If the scaffold layer, typically constructed from silicone, were made from other materials and considered to be a biopolymer matrix, cells would not be present in the non-channel areas.

Accordingly, Griffith and Singhvi do not teach or suggest multiple layers stacked on top of each other, where each layer comprises a polymerized biopolymer matrix capable of containing cells throughout the matrix as recited in the amended claims. For these reasons, Applicant requests that the rejections under 35 USC 103 be withdrawn.

Conclusion

In view of the foregoing, it is submitted that this case is in condition for allowance, and passage to issuance is respectfully requested.

If there are further issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time. It is believed that this submission does not require the payment of any fees. However, if this is incorrect, please charge any deficiency to Deposit Account No.07-1969.

This response is accompanied by a Petition for Extension of Time (one month) and a fee of \$60.00 as required under 37 C.F.R. 1.17. If the amount submitted is incorrect, however, please deduct from Deposit Account No. 07-1969 the appropriate fee for this submission and any extension of time required.

Respectfully submitted,

/michaelcurtis/

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